A METHOD OF INDUCING OR ENHANCING CHONDROGENESIS WITH EXTRACELLULAR MATRIX CONTAINING BMP-4

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Background of the Invention

The limited capacity of articular cartilage to regenerate represents a major obstacle in the management of degenerative and traumatic joint injuries. The maintenance of a functional joint surface requires that articular chondrocytes respond to extracellular signals that are generated from growth and differentiation factors, mechanical stimuli, and interactions with specific components of the extracellular matrix. The invention is directed to an extracellular matrix of type I collagen, type II collagen, type I collagen plus hyaluronate, or type II collagen plus hyaluronate, and bone morphogenetic protein-4 (BMP-4). A combination of BMP-4 with differentiation factor-5 (GDF-5)is also useful.

Coordinated function of many cell types is regulated by integration of extracellular signal derived from soluble factors inducing growth factors and insoluble molecules such as extracellular matrix (ECM). The skeletal elements of the vertebrate limb are derived during embryonic development from mesenchymal cells, which condense and initiate a differentiation program that result in cartilage and bone. Bone morphogenetic proteins may play a crucial role in mesenchymal condensations in skeletal patterning, including the process of joint formation.

Despite the importance of joint formation in skeletal patterning and human disease, relatively little is known about the molecular mechanisms that control where and when a joint will form. In the limb, joints typically arise